

Thank you for inviting me.

I hope this title is sufficiently provocative. For many people, this hypothesis, that too much sleep can be bad for you, flies in the face of everything that they believe.

If that's true for you, then I hope to expand your outlook.

I would like to tell you a story, by Dr. Daniel Ezekiel. It appeared in this month's issue of The Canadian Journal of Diagnosis.

Read story...

Before beginning, let me emphasize that the insomnia I'm talking about is primary insomnia, and not sleeping problems causedby too much caffeine, severe pain, extreme anxiety, or medical conditions such as sleep apnea.



This slide shows the three hypotheses that I will be talking about. You will notice the term REM sleep in the second hypothesis. REM stands for Rapid Eye Movement; Rapid Eye Movement sleep, also called paradoxical sleep, occupies about 20 or 25% of our total sleep. It's the phase of sleep during which most of our dreaming takes place. I'll talk about it more later on.



First, let's consider insomnia. Never mind endemic, some people think there's an epidemic.

In some groups, the problem is very common. Fifty percent of elderly people in rural areas complain of insomnia; 40% of community-dwelling Alzheimer patients have disrupted sleep. Severe insomnia is very common in cancer patients.



In addition to subjective distress, insomniacs are also poorly adjusted when studied by objective measures, such as the MMPI. Depression and anxiety are frequent.



Insomniacs use health care resources more. There are significant medication costs: in one study, 14% of the general population reported taking a hypnotic nightly. For clinic outpatients, this percentage rose to 24%.

Insomniacs have 2.5 times more automobile accidents than good sleepers. Over half of sleep clinic clients have had accidents at work, and almost half were involved in motor vehicle accidents.

Users of sedative or hypnotic medications have more motor vehicle accidents, and visit emergency rooms more frequently.

Dr. Roland Grad, at this hospital, showed that long-acting benzodiazepines significantly increase the risk of hip fracture in the elderly.

In terms of occupational performance, dalmane reduces performance the following day. Insomniacs have higher rates of substance use disorder, itself associated with poor occupational performance, and take more sick leave.



Let's talk about fatigue. I work with oncology patients, and I can attest to the finding of many studies in which cancer patients reported fatigue to be their most distressing symptom.

Almost 80% of rheumatoid arthritis patients are affected by fatigue. In hemodialysis patients, fatigue is related to inactivity and sleep disturbance.

In chronic fatigue syndrome, 28% of patients described their fatigue as so severe that they became bedridden, able to do almost nothing. Most patients with this syndrome are unable to work fulltime, and many receive disability payments for long periods of time.

20% of AIDS patients reported that their fatigue was responsible for having stopped working.



What does insomnia mean to you? For most people, and this includes researchers in the field, insomnia means not getting enough sleep. So what do insomniacs do? They go to bed earlier, stay in bed later, and take naps, all in an attempt to "get enough sleep". The slide shows two typical definitions of insomnia which reflect popular beliefs.

What's the reality? Studies show that insomniacs typically sleep as much as normals, and sleep more during the day.

Many individuals voluntarily extend their sleep time when the opportunity presents itself, eg on weekends or vacations, when ill, or upon retirement, even though they are aware that they function adequately with the amount of sleep they obtain on work or school days. When feeling fatigued, the usual tendency is to sleep more. Knowledge that for anything else that the body needs; for example, food, water, vitamins, minerals, exercise, or sun, an excess is usually detrimental, does not automatically apply to sleep. Sleep, Depression, and Fatigue



What's the meaning of fatigue? Does it mean the feeling you get after running a marathon, or writing a six-hour exam? Does it mean the drowsy sensation you experience at 2 in the afternoon after a big lunch with a little wine? Or is it the lack of energy, the "blah" feeling, that cancer patients and depressed patients complain of? Unfortunately, it can mean all of these things, again, both to the general public and to researchers in the field.

I would like to suggest the following terminology:

<u>Acute fatigue</u> is the feeling after hard physical or mental exertion. It gets better with rest, and of course, sleeping is a good way to rest, but it's not necessary to improve acute fatigue.

<u>Sleepiness or drowsiness</u> occurs normally for most adults in the early afternoon, even if they're getting enough sleep, and will occur at other times if you're <u>not</u> getting enough sleep. If you have the opportunity to nap, drowsiness can be quite a pleasant feeling. Daytime sleepiness can even be objectively measured, using what's called the Multiple Sleep Latency Test.

Finally, there's <u>chronic fatigue</u>. This is the dragged out feeling which isn't helped by rest or by sleep, which is so common in depression and in medical illness. Most people believe that this kind of fatigue is caused by lack of sleep. My hypothesis is that too <u>much</u> sleep, and in particular too much REM sleep, is the cause of chronic fatigue.



I'm going back to insomnia. My apologies for jumping back and forth; I'm still trying to figure out a nice, cohesive way of presenting these ideas.

Why do I think that insomnia has little to do with lack of sleep, and instead that difficulty falling asleep or staying asleep is caused by the person sleeping longer than they need?

It's known that insomniacs sleep as much as normals, but spend more time in bed. They underestimate the amount they actually sleep, in some cases to extreme lengths. There's a case in the literature of a woman who insisted she had not slept at all, for 13 years! In the sleep lab, she slept 7 1/2 hours, but the next morning she again was convinced she had not slept a wink the entire night. Obviously, most insomniacs do not suffer from such an extreme lack of reality testing.

Insomniacs demonstrate less daytime sleepiness, as measured by the Multiple Sleep Latency Test, and they have better reaction times. Both indicate a degree of alertness consistent with getting more than enough sleep.



In what situations might people sleep excessively? Some people simply need less sleep, but are convinced that they should have the usual 7 or 8 hours. They will therefore spend at least 7 or 8 hours in bed, and some of that time will be spent tossing and turning.

A number of studies demonstrate that as we get older, we need less sleep. Many people are unaware of this, or may even believe that they need more sleep as they age, and thus increase their time in bed. For example, in one study nursing home residents were found to spend 12 hours out of every 24 in bed, even though they slept only 6.2 hours on average.

When people become ill, they frequently sleep more. In bacterial or viral infections, various sleep-promoting agents are produced by the body, such as interferon and the interleukins. Bacterial cell wall substances have also been found to induce sleep. Being hospitalized, or taking time off work or school, gives opportunities for more sleep. Chronic fatigue associated with illness may be interpreted as indicating that more sleep is necessary. Spending more time in bed promotes insomnia.

Finally, people without regular employment or school commitments, including retirees, have more opportunities for earlier bedtimes, later rising times, and daytime naps. Too much time in bed perpetuates insomnia as do irregular arising and retiring times and napping, according to some studies. Sleep, Depression, and Fatigue



Now, let's get back to REM sleep. REM sleep occurs at specific times throughout the night, at intervals of about 90 minutes; that is, about 4 or 5 cycles per night. It follows a circadian rhythm, with a minimum in the early evening, and increasing through the night to a peak in the morning around 8 o'clock. During the day, if you were sleeping, REM% would gradually decrease back to its minimum in the early evening. Imagine a sine wave.

Thus, longer total sleep means more REM sleep, but the timing of your sleep is very important. Sleeping in in the morning generates considerably more REM sleep than going to bed earlier, even if the total sleep time is the same.

Now, some REM sleep is essential for learning, and specifically for the consolidation of long-term memory. Perhaps this is why infants sleep so long; they're continually learning new things, whereas the elderly encounter much less in the way of novelty each day. Because the amount of REM sleep as a percent of total sleep remains remarkably constant throughout the life span, at about 20 to 25%, the elderly need less total sleep to get the smaller amount of REM sleep they require.



The association between increased REM sleep and depression has been noted by a number of researchers, but the hypothesis that too much REM sleep may cause depression was first published in 1987 by Wiegand and colleagues.

I've collected lots of papers which provide support for this hypothesis. I've grouped the evidence into a number of categories, as shown on this slide.



First, let's look at what happens if we increase REM sleep. Some medications such as reserpine, an antihypertensive, and the benzodiazepines, increase REM sleep. These medications have depression as a side effect.

If you sleep deprive a depressed person, their depression disappears. You can get the depression to reappear quite reliably by allowing the person to have a nap which is long enough to include REM sleep.

Less helpful in demonstrating cause and effect are the large number of studies which look at various symptoms associated with increased REM sleep.

For example, REM sleep is higher in depressed persons, and in relapses of depression following successful antidepressant treatment. However, it is important to point out that many depressed patients have other REM sleep abnormalities, including short REM latencies and more REM sleep during the early part of sleep. Short REM latency, which suggests increased REM sleep, is also found in many patients with illnesses such as narcolepsy, schizophrenia, obsessive-compulsive disorder, mania, chronic psychogenic pain sndromes, drug withdrawal states, and posttraumatic stress disorder. Many of these disorders include depressive symptoms, and may respond to antidepressant treatment.



As I mentioned earlier, Wiegand and his coworkers were the first people (at least, that I was able to find) to propose that too much sleep can cause depression. Of course, sleeping longer will increase REM sleep too.

However, Globus had employed the concept of the "worn out" syndrome as early as 1969 to describe the "tired, lethargic, irritable, fuzzy thinking, difficulty getting started" state which occurred in students after a night of sleep prolonged to 10 or more hours. Other researchers have found that sleep prolongation impairs mood and performance, and that long sleepers have poorer psychological adjustment than short sleepers.

Taub and his coworkers have also demonstrated performance deficits after extended sleep.

Melatonin, which is all the rage south of the border, is known to increase sleep duration, but it also increases subjective feelings of fatigue.



Besides the effects of increasing the amount of sleep, there are a number of findings associated with increased sleep. For example, hypersomnia is characteristic of bipolar depressions, and is also found in young depressives, in seasonal affective disorder, and in chronic fatigue syndrome. Depressed people underestimate their sleep length and frequently nap. These people also have longer sleep latencies and lower sleep efficiencies, suggesting excessive sleep.

People with cancer, depression, fibromyalgia, systemic lupus erythematosus, and HIV infection sleep more and nap more, perhaps causing their high levels of fatigue.

Nursing home patients show increasingly impaired skills in activities of daily living as their total sleep hours increase.

Finally, a large-scale epidemiological study showed that people who slept 9 hours or more had poorer physical health and a higher mortality.



As we saw earlier, because REM sleep peaks in the morning, probably related to the timing of sunrise, sleeping later will increase REM sleep even if total sleep duration remains the same. Several researchers have found that late sleeping itself may aggravate or precipitate depression. Medical students who went to bed and arose later had abnormal MMPI scores.

Delaying sleep by six hours led to significant increases in subjective felings of depression as well as decreased alertness, happiness, and energy.

So much for the direct effects of sleeping later. Other observations include poorer performance on simulated clinical tasks by emergency room doctors who worked the night shift and slept during the day. A study of patients with delayed sleep phase syndrome showed that 45% were taking antidepressants, suggesting that delayed sleep is associated with depression.



I am again talking about insomnia, because of my hypothesis that insomnia is caused by sleeping excessively. Thus I would expect that insomniacs also have excessive REM sleep, and if too much REM sleep causes fatigue and other depressive symptoms, we might expect to find these symptoms in insomniacs.

Insomnia certainly is a risk factor for depression. A study involving almost 8000 respondents showed that people who continued to have insomnia over a one-year period had 40 times the likelihood of developing a new major depression compared to those without insomnia.

Fatigue and insomnia are closely linked in cancer, during cancer treatment, following heart attacks, in hemodialysis patients, in rheumatoid arthritis, and especially in chronic fatigue syndrome.



If the hypothesis about excessive REM sleep causing fatigue and other depressive symptoms is true, then one might reasonably assume that reducing REM sleep would improve these symptoms. Again, we can look at evidence in support of this idea by considering what happens when REM sleep itself is reduced, what happens when total sleep is reduced (which of course will also reduce REM sleep); and finally, the effects of sleeping earlier (which again reduces REM sleep because of its diurnal variation).



First, it is possible to selectively deprive people of REM sleep by waking them up each time the polygraph in the sleep lab shows that REM sleep is starting. In depressed people, this manoeuver was found to have an antidepressant effect equivalent to that of imipramine.

In terms of associated phenomena, it has been found that suppression of REM sleep and prolongation of REM latency are characteristic of antidepressant treatments, including most medications; electroconvulsive therapy; stimulants such as methylphenidate; and even exercise. Cognitive behavioural therapy for depression was found to decrease REM density. For tricyclic antidepressants, the amount of REM sleep suppression after the initial dose of medication predicts the amount of clinical improvement eventually obtained.



Total sleep deprivation, which clearly causes total REM sleep suppression as well, has been extensively studied. Here are some of the results:

in 60% of patients with major depression, total sleep deprivation leads to an immediate and substantial reduction of depressive symptoms. Total sleep deprivation can precipitate mania in patients with bipolar disorder and possibly also in previously normal individuals.

Sleep deprivation also was able to reverse a severe cognitive impairment in a patient with treatment-resistant depression, thus helping to differentiate pseudodementia from true dementia.

Partial sleep deprivation, particularly late in the sleep period, also has antidepressant effects, including in premenstrual dysphoric disorder. Task performance was shown to improve in some studies, while others showed no effect or worsening performance.

Finally, reducing sleep in demented elderly patients by preventing daytime naps improved sleep-wake disturbances.



Besides the effects of direct interventions that I just described, there are a number of associations, such as the observation that manic patients sleep less. Some antidepressants, for example clomipramine, reduce sleep by increasing sleep latency and early morning awakening.

I put this 18th century proverb on the slide, because several studies suggest that short sleepers are better adjusted psychologically than long sleepers.

Another interesting finding is that methylphenidate which as you know is widely used to treat attention deficit hyperactivity disorder, significantly reduces sleep duration. We also use this medication as an antidepressant in the elderly and in medically ill individuals.



You can treat depressed patients successfully with phaseadvance therapy, which consists of advancing their sleep period by several hours without reducing their sleep time.

Late partial sleep deprivation is antidepressant, whereas early partial sleep deprivation is not. This applies also to premenstrual syndrome.

I couldn't resist the quote by Ben Franklin...



Bright light is the most powerful external stimulus which can entrain the body's circadian rhythms. This suggests that the REM sleep peak which in one study was found to occur at 8:30 am, may in fact be synchronized to the time of sunrise.

Thus, arising at dawn may reduce the possibility of excessive REM sleep, while sleeping in the morning after sunup might just be a surefire way to experience too much REM sleep.

In precivilization, people slept when it was dark, and were driven by hunger to be up and about looking for food as soon as it was light enough to do so. Nowadays, urban societies no longer arise with the sun; we're tied to the clock. I would like to speculate that when the clock is set back in the fall, so that the sun rises an hour earlier, many people will all of a sudden experience an increase in their REM sleep. Is this a possible trigger for the winter depressions of seasonal affective disorder?



I certainly wouldn't want you to get the impression that all the studies support these hypotheses. There are certainly lots that seem to contradict these ideas. However, much of the research in this area is marred by shortcomings. For example, many studies fail to report either the total sleep time, or the time in bed.

Daytime naps are forbidden in some studies, but other studies fail to control for them. In either case, daytime sleep habits of subjects just prior to experiments are rarely reported.

Finally, many sleep lab studies impose standard conditions on subjects with respect to bedtime, arising time, and time in bed, conditions which may bear no relationship to their usual sleep patterns. Sleep, Depression, and Fatigue



OK, suppose with all of that, I've managed to convince you. Now what? What approaches might you use with your patients?

Over the past several years, many studies confirm that the most effective treatment for insomnia may be what's variously called sleep restriction or sleep compression. Essentially, both approaches reduce time in bed. It is also important to eliminate long daytime naps.

What do I tell patients? Depending on their age, I might suggest no more than 6 or 7 hours in bed, and to stick with the same times for retiring and arising from one day to the next. They must adhere to this even if they don't sleep at all during the night. If they feel drowsy during the day, they should nap, but not for more than 15 minutes.

For depressions, antidepressants may be indicated. Medications which suppress REM sleep may be more effective than those which do not. On the other hand, reducing or eliminating medications which increase REM sleep, such as benzodiazepines, may also be important.

When fatigue or other depressive symptoms present, and a detailed sleep history indicates that the person sleeps in the morning, say after sunrise, or later in the day, it may be worthwhile to ask him or her to get up early and stay up. A little caffeine daily helps elevate mood and keeps people awake. Occasionally hypersomnia and lack of energy can be treated with stimulants such as methylphenidate. Sleep, Depression, and Fatigue



Assuming that all of this works, what can we expect?

For individuals suffering from fatigue, insomnia, or other depressive symptoms, strategies to reduce REM sleep will improve mood, reduce chronic fatigue, improve energy and performance. If symptoms are due to excessive sleep, then a reduction in sleep will make more hours available each day for work or leisure pursuits.

On the other hand, when individuals sleep less, daytime drowsiness may become more frequent. This increases the risk for car accidents and accidents on the job. Short naps are effective at counteracting sleepiness, and employers may find that providing time and facilities for naps "on the job", may improve employee morale, job satisfaction, job safety, and productivity. Cars and factory equipment might need to be equipped with devices to detect operator drowsiness.

It may be, however, that a reduction in the use of hypnotic medication to treat insomnia will result in fewer medication-related accidents.

Adjustments in sleep timing and duration to control insomnia, fatigue, and depressive symptoms represent public health measures, and thus potentially could save money in medications, doctors' fees, and clinic costs. So why do I want to talk myself out of a job?



This all sounds very nice, but it needs some good sound research to either prove or disprove these hypotheses. Obviously, carefully controlled intervention trials are ultimately necessary, but this requires funding. Getting grants will be easier with pilot data.

I am fortunate to be working with Eva Libman, Catherine Fichten and their group, experts in the study of sleep disorders. We are in the process of putting up a questionnaire on the world wide web of the internet. This demographic study will attempt to find associations between sleeping patterns and depressive symptoms. While several thousand responses will certainly make us happy, there is the very real possibility that we might get half a million people to fill in our questionnaire. I'm sure you will want to take part, and I'll let you know when it's ready.

Thank you for listening. Sleep well!